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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,319	04/22/2005	Ellen J Baron	222310-US	9127

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,319	BARON ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5 and 6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is responsive to the Response and amendments filed January 21, 2009. Claim 1 has been amended. Claims 1 and 5-6 are now pending and under consideration. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons set forth below. Any rejections and/or objections not reiterated in this action have been withdrawn. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

3. Claims 1 and 5-6 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cockerill et al (US 7,074,598 B2 [11 July 2006; filed 25 September 2002]) in view of Tyrell et al (Journal of Clinical Microbiology 35(5):1054-1060 [May 1997]), for reasons given below and in the prior Office action of September 18, 2008. **It is noted that applicant's amendment of independent claim 1 to require performing "at least two of" the sub-steps now identified as a)-c) in claim 1 necessitated the new grounds now incorporated into this rejection.**

Cockerill et al disclose methods of detecting vancomycin-resistant *enterococci* in biological samples, which methods employ real time PCR (see entire reference, particularly, e.g., col 1, line 27-col 2, line 14; col 5, lines 3-34; and col 11, line 34-col 14, line 55). Cockerill et al disclose the analysis by their methods of samples including "anal or peri-rectal swabs, stool samples, blood, and body fluids" (see col 2, lines 66-67). Further, in detecting and determining the type of vancomycin-resistant enterococci

present in such samples, Cockerill et al achieve the objective of "detecting the presence of a bacterial pathogen in a clinical sample," as set forth in the preamble of independent claim 1. Cockerill et al disclose the analysis of both samples and nucleic acids extracted therefrom, including total RNA or DNA extracted from clinical samples (see, e.g., col 9, lines 16-30), and therefore disclose "at least partially isolating nucleic acid" as set forth in the first step of claim 1. Cockerill et al disclose real-time PCR that is monitored by analysis of hybridization probe melting temperatures, allowing the identity of the specific target sequences present to be both detected and quantitated (see, e.g., col 12, line 59-col 14, line 55); therefore, Cockerill et al teach "quantifying" and "monitoring" steps meeting the requirements of the claims with the exception of the identity of the target nucleic acid. Cockerill et al also exemplify the practice of their method in quantifying and "monitoring temperature dependence of hybridization" in detecting a "group of predetermined species of" a bacterial pathogen, specifically, vancomycin-resistant enterococci (see, e.g., Example 3). Particularly, Cockerill et al disclose that samples with positive signals at melting temperatures corresponding to the various positive controls employed allow determination of the presence of the target sequence indicated by the corresponding positive control, while samples having melting curves that are "not above baseline" are considered negative (see, e.g., col 20, lines 27-40). Thus, Cockerill et al inherently disclose that positive signals must exceed a certain level (i.e., the cut off value that allows the sample to be identified as "positive" based on correspondence with the positive control) to be considered positive, and that signals below baseline are considered negative. It is noted that the claims do not require, e.g.,

any particular manipulative steps of determining cut-off values prior to making comparisons, and that the analysis of data using LIGHTCYCLER software, as taught at, e.g., col 20, lines 28-29, requires comparisons with both a baseline value and positive control values that were determined prior to data analysis in order to make a determination with respect to whether a sample is positive or negative. Further, any sample that is "determined" to be positive is also simultaneously "determined" as not meeting the conditions of b) or c) of the claims, and any sample that is "determined" to be negative/below baseline is also simultaneously "determined" as not meeting either a) or b) of the claims. The claims recite "determining whether" an amount is above/below a value; thus, Cockerill et al's disclosure of detecting both positive and negative results with various samples are each sufficient to meet the requirements of the instant claims as written. With further regard to claims 5 and 6, it is again noted that Cockerill et al disclose the analysis of blood, and the analysis of *enterococci*, as set forth above.

Cockerill et al do not teach methods in which the 16S/23S spacer region is employed as an amplification/detection target, as required by the claims.

Tyrell et al disclose methods in which PCR amplification of the enterococcal 16S/23S spacer region is employed to detect enterococci, teaching that the method is "a reliable technique for species identification of enterococci" (see entire reference, particularly the abstract). In view of the teachings of Tyrell et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Cockerill et al so as to have adapted the method to permit rapid species identification of enterococci via real time, specific PCR

amplification of 16S/23S spacer sequences, either in addition to or instead of the *van* target sequences exemplified by Cockerill et al. An ordinary artisan would have been motivated to have made such a modification for the advantage of and in order to have achieved the predictable result of determining the species of enterococcus responsible for a particular infection, either instead of or in addition to determining whether the bacteria was vancomycin resistant. It is also noted that the practice of such a method would result in a method in which the "monitoring temperature dependence of hybridization" would be with respect to a 16S/23S spacer region and would be effective to detect "the presence of a group of predetermined species of said bacteria pathogen," as set forth in claim 1. It is further noted that as Tyrell et al disclose the sequences differences in the 16S/23S spacer region that characterize various enterococcal species, an ordinary artisan would have had a reasonable expectation of success in performing such methods.

With regard to the rejection of claims 1 and 5-6 set forth in the prior Office action, **the response traverses the rejection on the following grounds**. The response argues that the claims as amended require "at least two of" sub-steps a)-c) of claim 1, and that Cockerill et al does not teach or suggest a second predetermined cut off value as is required by the amended claims. The reply references page 9, lines 11-17 of the specification "for discussion on the utility and importance of the second predetermined cut off value". The reply further argues that Tyrell "does not provide teachings or suggestion relating to cut off values", such that the combination of references "does not provide all of the claim limitations". These arguments have been thoroughly considered

but are not persuasive. As is discussed in the rejection set forth above, Cockerill et al explicitly teaches a baseline value, and also inherently discloses a cut off value that is required to identify a positive sample. Thus, Cockerill et al does disclose two different values with respect to which samples are evaluated. Further, the claims as written recite "determining whether" an amount of nucleic acid is above or below two predetermined values; for any sample quantitated using the techniques of Cockerill et al, the measurements taken for that sample allow for the simultaneous determination as to "whether" the sample meets the requirements of a) and c) of claim 1. Thus, Cockerill et al does teach this aspect of the invention as claimed. Further, the "wherein" clauses of the claim are recited in the alterative, making clear that for any given sample one would draw only one conclusion; Cockerill et al teach both positive and negative samples, and therefore provide examples with regard to 2 of the 3 different scenarios encompassed by the claims (only one of which would in fact be required to meet the claims). The Tyrell reference is not relied upon with regard to any teaching of cut off values. Accordingly, applicant's arguments are not persuasive.

Conclusion

4. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Eyre et al (US 6,730,501 B2 [May 2004]) disclose improved methods of real time PCR (including methods using the LIGHTCYCLER platform; see entire reference, particularly column 6, line 27-col 7, line 37), and disclose determination of "positive", "negative" and "indeterminate" values in which "indeterminate" calls lie between the positive and negative cut off values (see col 13, lines 35-59).

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571/272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634